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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,131	KELER ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-33,36-39 and 46-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-33,36-39,46,47 and 49-62* is/are rejected.

7)☒ Claim(s) *48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 1/29/07 has been entered. Claims 1-26, 34-35, and 40-45 are canceled and new claims 46-62 have been added. Claims 27-33, 36-39, and 46-62 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Priority

Applicant's amendment to the specification provides the requisite reference to parent application 09/203,958, and includes the current status of this application.

Claim Rejections - 35 USC § 112

The rejection of claims 27-34 and 39 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in view of the cancellation of claim 34 and the amendments to claims 27-33, and 39, which are now limited to cells transformed to express an antibody or antibody binding fragment thereof that binds to an Fc receptor.

The rejection of claims 33 and 35-39 under 35 U.S.C. 112, first paragraph, for scope of enablement is withdrawn in view of the cancellation of claim 35 and the amendment of claim 33 to recite that the "first cell" is transformed "ex vivo".

Applicant's addition of new claims 46-47 has necessitated the following new grounds of rejection under 35 U.S.C. 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-47 are **newly** rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claims 46-47 depend on claim 27 and further limit the "first cell" to one which, "further comprises a transmembrane protein". The claim as written reads broadly on a cell which separately expresses an antibody which binds to an Fc receptor and a transmembrane protein. While the specification provides a description of nucleic acids encoding a fusion protein which comprises an antibody which binds to an Fc receptor operably linked to a transmembrane protein such as PDGF, the specification does not disclose or describe making a cell which has been transformed with two separate nucleic acids, one which encodes the antibody, and the other that

encodes the transmembrane protein. The specification further fails to disclose any cell that expresses the antibody as claimed and a transmembrane protein as separate proteins. It is noted that the applicant points to original claims 17-18 and pages 2 and 7 of the specification as providing support for new claims 46-47. However, original claims 17-18 were drawn to cells expressing a fusion protein. The disclosure on page 2 is also limited to a discussion of chimeric fusion proteins, while the cited section of page 7 only provides a definition of the term "transmembrane protein". As such, nothing in the specification discloses the breadth of the cells as now claimed in claims 46-47. Therefore, the subject matter of new claims 46-47 represents new matter not disclosed in the original specification as filed.

The rejection to claim 35 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the cancellation of the claim. The objection to claim 35 is also withdrawn in view of the cancellation of the claim.

The addition of new claims 47-48 has necessitated the following objection.

Claims 47-48 are **newly** objected to because of the following informalities: both claims recite "from from" in line 2. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The rejection of claims 27 and 31-35, and 38-39 under 35 U.S.C. 102(a) as being anticipated by WO 97/20048 (June, 5, 1997), hereafter referred to as Ledbetter et al., is withdrawn over canceled claims 34-35 and further withdrawn over the remaining pending claims in view of the newly added limitation that the anti-Fc antibody binding to the Fc receptor is not blocked by endogenous ligand.

Please note that amended claims 27, 31-35, and 38-39 are newly rejected below under 35 U.S.C. 103.

Claim Rejections - 35 USC § 103

The rejection of claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/20048 (June, 5, 1997), hereafter referred to as Ledbetter et al., in view of WO 91/00360 (January 10, 1991), hereafter referred to as Fanger et al., is withdrawn in view of the newly added limitation that the anti-Fc antibody binding to the Fc receptor is not blocked by endogenous ligand.

The rejection of claims 33 and 36-37 under 35 U.S.C. 103(a) as being unpatentable over WO 97/20048 (June, 5, 1997), hereafter referred to as Ledbetter et al. in view of Guyre et al. (1997) Canc. Immunol. Immunther., Vol. 45, 146-148, is maintained over claims 33 and 36-37 and is further applied to amended and new claims 27, 31-32, 38-39, 46, and 49-62. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

Please note that in regards to new claim 46, the transmembrane protein is not identified as being a recombinant protein or even as part of the anti-Fc receptor antibody fusion protein, but includes transmembrane proteins naturally expressed by the "first cell". As such, all mammalian cells express at least one naturally occurring transmembrane protein such as an ion channel.

As set forth in the previous office action, Ledbetter et al. teaches the construction of recombinant expression vectors which comprise a fusion protein comprising a single chain Fv molecule operatively linked to a transmembrane domain of a cell surface receptor and the use of said vector to transfect cells *in vitro/ex vivo* (Ledbetter et al., pages 6-7, page 12, lines 14-20, and page 21). Ledbetter et al. further teaches that the single chain Fv binds FcγR , FcαR, or FcεR, including CD64 which is FcγRI (Ledbetter et al., pages 6-7, bridging paragraph). Ledbetter et al. further teaches that the transfected cells expressing the single chain Fv fusion protein on the cell surface can be used in *ex vivo* or *in vivo* methods for enhancing a T cell response in a subject (Ledbetter et al., page 12). In particular, Ledbetter et al. teaches that autologous or allogeneic cells, such as tumor cells, are genetically modified to produce the scFV on the cell surface *ex vivo* and then administered to the subject to stimulate a T cell response (Ledbetter et al., page 12, lines 20-30). Please note that as mammalian subjects have effector cells and lymphocytes, administering tumor cells genetically modified to produce the sFV on the cell surface to a subject constitutes "contacting the cell with an effector cell in the presence of a lymphocyte". Note as well that a tumor cell naturally comprises tumor antigens.

Ledbetter et al. does not specifically teach the H22 antibody which recognizes CD64. Guyre et al. supplements Ledbetter et al. by teaching the H22 antibody and its use in generating fusion proteins with gp120 or tetanus toxin (Guyre et al., page 148, column1, paragraphs 2-3),

Guyre et al. provides motivation for using the H22 antibody in the single chain fusion protein taught by Ledbetter et al. by teaching that the H22 antibody binds to CD64 outside the ligand - binding domain of the receptor such that the binding of H22 is not inhibited by serum IgG (Guyre et al., page 148, column 1, paragraph 3). Thus, based on the motivation to use the H22 antibody in order to bind CD64 outside of the Fc binding domain as taught by Guyre et al., it would have been *prima facie* obvious to the skilled artisan to use the H22 antibody as the Fc binding portion of the chimeric molecules taught by Ledbetter et al. Further, in view of the high level of skill in molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success of making and using cells expressing a chimeric molecule comprising H22 according to the teachings of Ledbetter et al. in view of Guyre et al. to increase an immune response in a subject.

The applicant argues that Ledbetter fails to teach or suggest "..a method of increasing an immune response in a subject, as claimed by applicants (i.e. phagocytosis and lysis)". The applicant argues that the only teaching in Ledbetter of modified scFV molecules which remain attached to the cell surface is for the purpose of promoting adhesion between two lymphocytic cells, not for lysis or phagocytosis of a target cell by an effector cell. In response, while the applicant is correct in stating that the Ledbetter discloses that the purpose of the scFV molecules is for "adhesion", Ledbetter et al. clearly teaches that the activity of the scFV expressed by cells is for the stimulation of immune responses, and in particular T cell responses. Further, it is noted that the results of the adhesion between lymphocytes and non-lymphocytic cells mediated by anti-Fc receptor antibodies expressed by a cell are clearly dependant on the composition of the fusion protein. The binding of antibody to Fc receptor can result in several effects depending on

the identity of the Fc receptor and the identity of the cell expressing the Fc receptor. For instance stimulation of the Fc receptor on macrophages by the binding of anti-Fc antibody leads to phagocytosis. Therefore, applicants arguments are not compelling since the applicant's claims are not limited to any particular type of transformed cell, and since adhesion can result in different outcomes depending on the identity of the target receptor and the cell that expresses the target receptor. It is further noted that the H22 antibody taught by Guyre et al. binds to CD64 which is abundantly expressed by macrophages.

The applicant is also reminded that "Where the claimed and prior art products are identical or substantially identical in structure or compositions, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. MPEP 211.01 and In re Best, 195 USPQ 430, 433 (CCPA 1997). Further, "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 15 USPQ 2d 1655, 1658 (Fed. Cir. 1990). Please note as well that in *Titanium Metals Corp. V. Banner*, 227 USPQ 773 (Fed. Cir. 1985), the court states that it is immaterial what properties a particular composition has or who discovered the properties because if the composition in the prior art is the same as that claimed, it must necessarily exhibit these properties. Also, reliance upon inherency is not improper even though rejection is based on Section 103 instead of Section 102. *In re Skoner*, et al. 186 USPQ 80 (CCPA).

Therefore, applicant's amendments and arguments are not found persuasive and the rejection of record stands.

Amended claims 27-30 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/20048 (June, 5, 1997), hereafter referred to as Ledbetter et al. in view of Guyre et al. (1997) Canc. Immunol. Immunther., Vol. 45, 146-148, as applied to claims 27, 31-32, 38-39, 46, and 49-62 above, and further in view of WO 91/00360 (January 10, 1991), hereafter referred to as Fanger et al.

The combined teachings of Ledbetter et al. in view of Guyre et al., as discussed in detail above, provide the teachings, motivation, and reasonable expectation of success for making and using cells expressing a chimeric molecule comprising the H22 antibody to increase an immune response in a subject.

Ledbetter et al. differs from the instant invention by not teaching the administration of an agent to increase the expression of Fc receptors on effector cells. Fanger et al. supplements Ledbetter et al. by teaching that in a related method of inducing immune responses by targeting effectors cells with an antibody the binds to the Fc receptor, it is useful to pretreat the effectors cells, such as macrophages, with IFN-gamma and/or TNF, IL-2 and colony stimulating factor (Fanger et al., page 10). Fanger et al. provides motivation for treating the effector cells with IFN-gamma or other cytokines by teaching that IFN-gamma increases the number of Fc receptors for attachment to the targeting antibody and that cytokines such as TNF further activate the effector cell (Fanger et al., page 10). Thus, in view of the motivation to increase targets for antibodies specific for Fc receptors by treating cells with IFN-gamma provided by Fanger et al., it would have been *prima facie* obvious to the skilled artisan to further administer IFN-gamma to a subject to increase Fc receptor expression on effector cells and thus increase the number of

targets for cells expressing the sFV antibodies on the cell surface in the methods of Ledbetter et al. in view of Guyre et al. with a reasonable expectation of success.

Applicant's arguments regarding the teachings of Ledbetter et al. have been addressed in detail above. The argument that Fanger et al. does not remedy the deficiencies of Ledbetter et al. is further not persuasive as the office maintains that Ledbetter et al. does in fact teach methods of increasing immune responses as discussed above. Therefore, the instant rejection stands.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not

available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER